

CLAIMS

- 5 1. A micro-organism having a chromosome in which:
- a) at least one gene has been partly or wholly replaced by a homologous gene from another micro-organism, and
- b) an artificially introduced reporter gene is present and is expressed in a manner related to a homologous gene expression product.
- 10 2. The micro-organism of claim 1, wherein the gene is involved in DNA replication, RNA synthesis, protein synthesis, cell wall synthesis, transport or cell division.
- 15 3. The micro-organism of claim 1 or claim 2, which is a bacterium.
4. The micro-organism of claim 3, wherein the bacterium is a *Bacillus* strain capable of growth and sporulation and in which at least one
- 20 gene has been partly or wholly replaced by a homologous gene from another bacterium.
5. The *Bacillus* strain of claim 4, wherein:
- a) a *spoIIIE* gene has been replaced by its homologue from
- 25 another bacterium, and
- b) two reporter genes are present each linked to a promoter and responsive to the action of σ^F during sporulation, a first reporter gene being located in a segment of the DNA that is trapped in a prespore compartment when *SpoIIIE* function is impaired, and a second reporter gene being
- 30 located outside the said segment.

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6. The *Bacillus* strain of claim 5, wherein a *spoIII*E gene has been partly or wholly replaced by a homologous gene from *Streptococcus pneumoniae*.
- 5 7. The *Bacillus* strain of claim 4, wherein:
- a) a cell division gene has been partly or wholly replaced by its homologue from another bacterium, and
- b) two artificially introduced reporter genes are present, a first reporter gene having a promoter which is dependent on active σ^F or σ^E
- 10 factors, and a second reporter gene which provides a measure of the synthesis of the (inactive) σ^F or σ^E factor.
8. The *Bacillus* strain of claim 4, wherein the strain is modified by a mutation of a *spoIII*E gene which blocks transfer of the prespore
- 15 chromosome, and:
- a) a *spoOJ* gene has been replaced by its homologue from another bacterium, and
- b) one or two reporter genes are present, a first reporter gene having a promoter which is dependent on σ^F factor and placed at a location
- 20 where impaired *SpoOJ* function leads to increased trapping and hence to increased expression in the prespore, and/or a second reporter gene having a promoter which is dependent on σ^F factor and placed at a location where impaired *SpoOJ* function leads to reduced trapping and hence to reduced expression in the prespore.
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9. The *Bacillus* strain of any one of claims 4 to 8, which is a *B. subtilis* strain.

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10. A method of assessing an agent for antibiotic activity, which method comprises incubating the micro-organism of any one of claims 1 to 4 in the presence of the agent, and observing expression of the reporter gene or genes.

11. The method of claim 10, wherein the *Bacillus* strain of any one of claims 4 to 9 is induced to sporulate in the presence of the agent.

12. A method of determining whether an agent inhibits SpoIIIE function in *Bacillus* species, which method comprises inducing the *Bacillus* strain of claim 5 or claim 6, to sporulate in the presence of the agent, and observing expression of the first and the second reporter genes.

13. A method of determining whether an agent inhibits cell division in *Bacillus* species, which method comprises inducing the *Bacillus* strain of claim 7 to divide asymmetrically, as during sporulation, in the presence of the agent, and observing expression of the first and second reporter genes.

14. A method of determining whether an agent inhibits SpoOJ function in *Bacillus* species, which method comprises inducing the *Bacillus* strain of claim 8 to divide asymmetrically, as during sporulation, in the presence of the agent, and observing expression of the first and/or the second reporter gene.

15. The method of any one of claims 11 to 14, wherein the *Bacillus* strain is induced to sporulate and is contacted, just prior to asymmetric cell division, with the agent.

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16. A panel of the micro-organisms of any one of claims 1 to 9, wherein in different members of the panel genes have been partly or wholly replaced by homologous genes from different micro-organisms.

5 17. A method of assessing an agent for antibiotic activity, which method comprises incubation of the members of the panel of claim 16 in the presence of the agent, and observing expression of the reporter gene or genes in different members of the panel.

10 18. A method which comprises incubating a micro-organism of any one of claims 1 to 9 in the presence of an agent, observing expression of the one or more reporter genes and thereby determining that the agent inhibits the growth of the micro-organisms, and using the agent as an antibiotic.

15 19. A method of killing or inhibiting the growth of bacteria, which method comprises contacting the bacteria with an agent which inhibits the growth of a micro-organism of any one of claims 1 to 9.

add B1

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A2
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